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Impact of the life sciences on organisation and management of R&D in large pharmaceutical firms

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Abstract: The life sciences are having a significant impact on the organisation and management of R&D in large pharmaceutical firms, as well as restructuring the markets for new therapeutic products. However, there is continuing scepticism about large firms' ability or inclination to build in-house capacity for biologics and extract value from the life sciences. This paper explores the effect of life science innovation on early and late-stage R&D, and considers the implications for strategic management and the transition of compounds through the middle stages of the R&D pathway. The analysis, which includes two company case studies, reveals that new life science technologies have had a marginal impact on late-stage R&D, but companies are exploring new organisational or translational models to better exploit the science and reduce the phase 2 attrition rates. Findings suggest that firms have the capability to adapt to a new innovation trajectory, but external pressures on strategic and organisational management will continue to determine the level and rate of success.

Keywords: pharmaceutical industry; life sciences; innovation; strategic management; R&D; translational medicine; biotechnology; organisation.

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Biographical notes: James Mittra is currently a Research Fellow and a Lecturer at the ESRC Innogen Centre, University of Edinburgh. His research is focused on the impact of the life sciences on the evolution of the pharmaceutical industry, regulation and policy processes for new technologies, such as stem cells and developments in the emerging field of translational medicine. He is also part of the course development team for the University of Edinburgh's first online postgraduate course in Translational Medicine.

1 Introduction

New discoveries in life science are having a significant impact on innovation in the pharmaceutical and health-related industry sectors. The promise of genomics and related areas of fundamental science is that drug discovery and approval processes will be

expedited, and that drugs will become more cost-effective and of greater therapeutic benefit to patients. The complexity of the biomedical paradigm, and the significant but diverse implications biotechnology and genomics have for various parts of the R&D pathway, has created intricate innovation systems and networks (Chiesa and Toletti, 2004; Dosi et al., 1988; Edquist, 1997). Large, incumbent pharmaceutical companies are increasingly reliant on the knowledge, products and expertise of external innovators as their traditional capabilities in small molecule drug development no longer appear sufficient to sustain productivity (Mittra, 2007). However, there is emerging scepticism about the revolutionary claims made on behalf of the life sciences as pharmaceutical companies have failed to deliver radically new therapeutic products following the mapping of the Human Genome (Arundel and Mintzes, 2004; Hopkins et al., 2007; Mittra, 2005; Nightingale, 2000; Nightingale and Martin, 2004). Questions remain about the extent to which large firms have the capability and/or inclination to fully exploit the potential of biotechnology and genomics, by restructuring internal R&D processes and therapeutic foci, for example, so that high value products are successfully delivered to market.

This paper explores the impact of life science innovation on the changing organisation and strategic management of R&D. Methodologically, it draws on the author's original interview data from senior scientists and managers within large pharmaceutical companies; secondary commercial data on technologies and therapeutic trends and two rich company case studies that illustrate different strategies for responding to innovation deficit through the exploitation of translational research models.¹ This paper reveals both endogenous and exogenous commercial and technological challenges facing large firms, which impact on their ability to successfully exploit emerging biomedical knowledge and new translational processes for drug discovery and development. The data suggest that new technologies have created economies of scale in early-stage R&D yet, despite huge investment in biotechnology and genomics, the perception of innovation and productivity deficit remains prevalent. Furthermore, the attrition rate of compounds in phase 2 is significant and has induced firms to experiment with creative organisational strategies. Industry is optimistic that decentralised R&D models, coupled with a reassessment of conventional technological and therapeutic priorities, will enable it to successfully respond to challenges posed by tumultuous social, technological and commercial externalities. The concept of 'translational medicine' is increasingly being used to describe these new organisational processes for expediting the movement of compounds from 'bench to bedside' (Horig and Pullman, 2004; Mankoff et al., 2004).

This paper is structured as follows. Section 2 illustrates the key changes that have taken place in pharmaceutical innovation and some of the generic challenges facing large firms. These challenges have provided the primary impetus for major organisational restructuring and experimentation with new technologies and strategic management options. Following from this, in Section 3, I explore large firms' investment in life science technologies as a means of exploiting economies of scale and scope in the discovery and early stage development of novel compounds. Interview data reveal how firms have responded to the transformative potential of the life sciences and uncover scientists and managers' perspectives on the future commercial benefits and key innovation bottlenecks. One main finding is that new technologies have not yet yielded significant returns in late-stage R&D, and important questions remain about firms' ability to extract optimal value from the life sciences. Section 4 presents two company case studies that highlight some of the different ways in which large firms are exploiting new

organisational and strategic management options to sustain innovation and reduce the attrition rate of novel therapeutic compounds. The first case study explores the reorganisation of R&D at GlaxoSmithKline; specifically the implementation of decentralised Centres of Excellence for Drug Discovery (CEDD). The second case study looks at the recently established Translational Medicine Research Collaboration (TMRC); a novel public–private partnership involving the global pharmaceutical firm Wyeth, Scottish Enterprise (a regional development agency), four Scottish universities and the NHS in a collaborative search for novel biomarkers. In Section 5, I critically explore some of the broader implications of these diverse organisational models and strategic choices for the future of ‘Big Pharma’ and therapeutic innovation.

2 The changing face of pharmaceutical innovation and key challenges facing industry

The pharmaceutical industry is an innovation-driven, R&D intensive sector susceptible to ‘technological shocks’ in the form of new scientific paradigms and path breaking technologies; where strategic options are shaped by a strong regulatory regime that exists outside the core innovation system (Tait, 2007). The success of multinational companies depends on a continual flow of new, innovative, preferably small-molecule ‘blockbuster’ therapies to sustain revenue growth. Genomics and biotechnology-related technologies and approaches that have or could transform pharmaceutical innovation include:

- 1 automated high-throughput screening and combinatorial chemistry to increase the rate of discovery for New Chemical Entities (NCEs)
- 2 systems biology and bioinformatics databases to aid understanding of the genetic basis of disease, which requires closer collaboration between medicinal chemists, biologists and IT specialists
- 3 pharmacogenetics to screen potential drug candidates and improve their safety and efficacy profile before they enter clinical development
- 4 recombinant proteins, monoclonal antibodies, peptides and large, organic molecules as drug candidates, which may require radical rather than incremental changes in manufacturing, regulation and distribution processes.

Here, one must distinguish large, protein-based molecules from new small molecules in terms of their impact on conventional innovation processes. Companies have attempted to apply these techniques to various stages of R&D, although the most significant changes have been in the discovery and preclinical phases. This will be elaborated further in the following section.

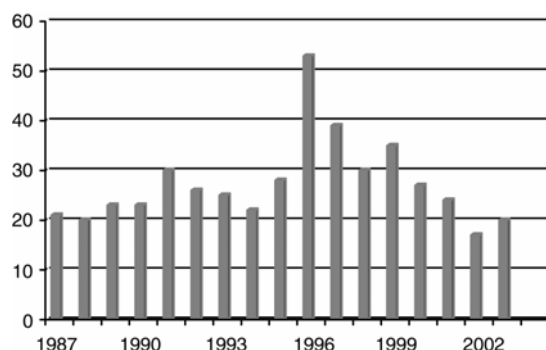
Before the emergence of the life sciences, and the expectations and ‘promissory visions’ it offered to industry (Borup et al., 2006), conventional, chemistry-based pharmaceutical R&D rested largely on serendipity as companies would screen known compounds stored in their extensive chemical libraries. Lead molecules would then be optimised by medicinal chemists to produce potential drug candidates; the most promising of which would then be moved to late-stage development and finally

to market. In the 1980s and 1990s, the R&D process was advanced considerably with the advent of molecular biology, synthetic chemistry and improvements in the development of screening technologies. These techniques increased the rate at which new molecular entities could be discovered and furthered industry's knowledge of disease and drug targets (Ratti and Trist, 2001). High capacity screening and better target identification and validation tools were invaluable to the pharmaceutical industry during this period. Nightingale (2000) suggests that biotechnology helped create 'economies of scale' in R&D as new technologies allowed companies to significantly increase screening capacity with less human resource and thus reduce the overall operating costs of drug discovery. He argues that both chemistry and biology shifted from essentially craft-based, sequential processes on single compounds to automated mass-production processes conducted in parallel.

The development of a wide range of life science technologies to improve the R&D process, and exploitation of a more rational approach to drug design, engendered a broader restructuring of the pharmaceutical industry (Drews, 2000; Mittra, 2007). In particular, large, vertically integrated pharmaceutical firms came to increasingly depend on the knowledge, expertise and products of external innovators, such as the new dedicated biotechnology firms and academic research institutions (Mittra and Williams, 2007). New technologies engendered significant organisational restructuring and subsequent changes in the innovation value chain (Quéré, 2003). Pharmaceutical R&D became characterised as a distributed or networked innovation system (Cambrosio et al., 2004; Chiesa and Toletti, 2004), in which the incumbent firms began increasingly to exploit merger and acquisition activity, strategic alliances, outsourcing and licensing models to sustain innovation (Crossley and Kordel, 2002; Langley et al., 2005; Mittra, 2007; Tait and Mittra, 2004). Coombs and Metcalfe (2002) suggest that large pharmaceutical firms now had to create, coordinate and combine a diverse range of research and development 'capabilities', alongside the normal processes of organic growth, to remain competitive and profitable.

Although the life sciences have provided the pharmaceutical industry with new strategic options and dynamic technological capabilities (Hilliard and Jacobson, 2003; Teece et al., 1997), it is important to recognise that the reshaping of the industry, and experimentation with new organisational models, has taken place in the context of much broader social, commercial and technological challenges. Despite the development of new technologies, and the potential panacea they promised to an industry that must continually innovate to survive, a number of internal and external factors threaten to undermine large firms' historic dominance in therapeutic innovation. In summary, the key challenges include:

Decline in R&D productivity: despite year-on-year increases in R&D expenditure, the pharmaceutical industry is plagued by a productivity crisis and a widespread perception of innovation deficit (Drews and Ryser, 1996). Although overall investment in pharmaceuticals tripled during the 1990s to more than \$30 billion, a declining number of new therapies were approved by regulators and placed within the market. Figure 1 reveals the number of NCEs approved by the FDA between 1987 and 2003, and Table 1 shows the domestic and total R&D spend as a percentage of sales for PhRMA member companies from 1971 to 2003.

Figure 1 NCE approvals 1987–2003

Source: FDA and Deutsche Bank AG Report.

Table 1 R&D as a percentage of sales: PhRMA member companies 1971–2003

Year	Domestic R&D as % of domestic sales	Total R&D as % of total sales
2003	18.3	15.7
1999	18.2	15.5
1995	20.8	16.7
1991	17.9	14.6
1987	17.4	13.4
1983	15.9	11.8
1979	12.5	8.6
1975	12.7	9.0
1971	12.2	9.0

Note: This data only shows R&D and sales within the USA.

Source: Adapted from PhRMA annual membership survey 2005.

Despite a peak in 1996, the number of approvals has been in general decline ever since. Furthermore, the number of new active compounds discovered by large pharmaceutical firms has remained relatively constant at 4–6 per year, despite significant advances in screening technologies and generally increased R&D expenditure until the mid 1990s, when internal R&D spend appeared to level off. This may be indicative of an increase in R&D outsourcing and/or higher reliance on licensing strategies from 1995. With few exceptions, most of the major, vertically integrated pharmaceutical firms are no longer generating in-house a sufficient number of new compounds to sustain revenue growth (Horrobin, 2001).

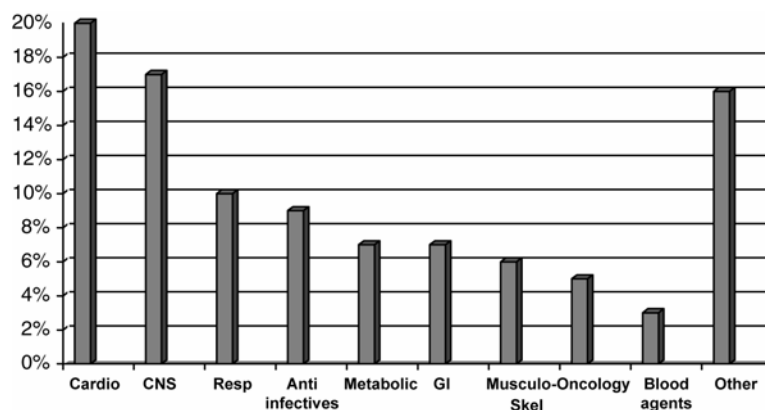
High attrition rate: although there has been great investment in new technologies, there continues to be a high attrition rate in pharmaceutical R&D, particularly in the middle stages of the R&D process and phase 2 clinical studies, where the success rate has been as low as 20%. Lack of demonstrable safety and efficacy appear to be the primary causes of attrition. Currently, only one in two compounds that enter phase 3 clinical trials eventually reaches the market. Reasons for the high attrition rate include: the complexity of the science and limited understanding/validation of new drug targets; a robotic approach to R&D has replaced a more intellectual approach (Drews and Ryser, 1996) and large firms face substantial problems of resource allocation and portfolio management. The bureaucratic organisational structure of large companies makes it

difficult for them to be nimble and reactive to new and potentially disruptive technological paradigms. As the small-molecule innovation model has reached a level of maturity, all the simple drug targets have already been discovered and are now coming off-patent. Companies must better utilise new technologies, innovative science and organisational capabilities to mitigate the attrition and productivity crisis.

Rising cost of drug discovery: new methodological approaches; internationalisation of research; integration of new disciplines/technologies (Howells, 2002) and successful knowledge management add to the overall costs of drug discovery. The cost for a large pharmaceutical firm to bring one product to market has been estimated to be around \$800 million (DiMasi et al., 2003). There are also increasing demands from regulators and healthcare providers to improve safety and efficacy and reduce the price of new innovative drugs in response to rising stakeholder expectations. Controversies over clinical trial data (McCrea and Markle, 1984), the safety of medicines and their therapeutic value (Abraham and Davis, 2007) and pharmaceutical firms' ostensible influence on regulatory processes (Kerridge et al., 2005; Sweet, 2004) are becoming increasingly common. The necessarily high 'regulatory hurdle', and often capricious nature of policy and regulation for new pharmaceutical products, continues to render fully integrated therapeutic R&D prohibitively expensive for all but the largest companies. Regulation has been shown to have a direct and significant effect on drug lead times and R&D performance (Dove, 2003; Hartley and Maynard, 1982) and limits the ability of 'new entrants' to compete effectively with the incumbent multinationals (Tait, 2007). Of course, some genomics-based companies have been successful in transforming themselves into competitive, fully integrated drug development companies (Rothman and Kraft, 2006), but they continue to be the exception rather than the norm.

Continued reliance on 'blockbuster drugs': although new life science technologies provide an opportunity to develop more targeted therapies for niche markets, the traditional blockbuster model of drug development remains prevalent amongst the larger firms. Companies continue to focus on a narrow range of therapeutic areas that generate high value and high demand products. Figure 2 provides data on the pharmaceutical market by therapeutic category, which suggests that large firms must have a strong presence in at least three or four key markets if they are to remain competitive and sustain revenue growth.

Figure 2 Pharmaceutical market by therapeutic category



Source: IMS Health and Deutsche bank estimates.

Consequently, the pharmaceutical market continues to be saturated with ‘me-too’ therapies or ‘incremental innovations’ in core therapeutic franchises, rather than ‘first in class’ products for a broader range of disease indications. Although there is a growing belief that the blockbuster model is unsustainable, no effective alternative has yet emerged. The expiry of many patents on existing blockbuster drugs is also amplifying concerns over productivity. Furthermore, the high cost to firms of traversing the increasingly onerous regulatory system means that the search for blockbuster therapies continues at present to be the only realistic strategy for a large firm to pursue.

Together, these industry challenges are fundamentally affecting the evolution of the pharmaceutical sector, as well as the strategic management of internally- driven R&D within individual companies. Firms must experiment with new technologies and managerial approaches to sustain innovation in the context of a turbulent social, political and commercial environment. The following sections elaborate these key issues in the context of specific firms’ managerial and organisational stratagems.

3 Extracting value from new life science technologies: the experience of large firms

The interview accounts of senior scientists and managers in large pharmaceutical companies reveal the fundamental changes that have taken place in the R&D process. Respondents countenanced the view that new technologies had helped create economies of scale in early stage R&D and rendered parts of the research endeavour more efficient by facilitating better capacity utilisation. A number of specific technologies were cited by respondents as having been particularly auspicious for early-stage R&D.

Firstly, general automation technologies, such as combinatorial chemistry and automated synthesis, have allowed large firms to increase the number of potential small molecule compounds available for downstream development. This has engendered a move away from the conventional craft-based design of single molecules to parallel, high-throughput screening processes. On the biological side, according to one respondent,

“there have been massive strides in trying to break down the process and identify the involvement of particular targets, enzymes and receptors in diseases and screening for them in a much more controlled way.” (Portfolio Manager, INT3/Company B)

These approaches have been exploited for both new biological and conventional small-molecule chemical entities. In one sense, automation technologies have enabled companies to disaggregate the components of biological and chemical systems – a highly reductionist approach – and generate high-level data to support candidate selection and optimisation. Another respondent stated:

To make a molecule which is selective, has the right pharmacology and is potent at its target is a process which is much quicker and much slicker than it was before. We are also beginning now – through chemical and in vitro methods – to address issues such as metabolism, which is now handled quite early in the process so that failures due to poor kinetics and metabolism in man have really decreased a lot over the last 10 years (Head of Neuroscience, INT9/Company D).

The availability of a broad spectrum of automation technologies – a large number developed by small and medium sized platform technology firms – have, according to interview respondents, significantly advanced the discovery and selection of viable therapeutic compounds.

Secondly, technologies such as X-Ray crystallography and electron microscopy have been invaluable for improving identification, knowledge and understanding of complex biological structures. While automated processes appear to have helped firms discover new molecular entities more cheaply and efficiently, these additional technologies have made a significant contribution to what is often referred to as rational drug design, which requires changes in the nature of R&D and its organisational structure (Cockburn, 2004). Respondents considered these technologies to have been particularly important for small-molecule drug development, as they have provided knowledge and understanding that have allowed organic chemists to design molecules that interact with specific drug targets in more predictable and efficacious ways. One respondent claimed that these technologies have allowed firms to “move away from the empirically-based approach to R&D, which had been very successful, towards a more target-driven, focused, disease pathogenesis underpinning” (Head of R&D Policy, INT1/Company 1). Another respondent claimed that a variety of analytical technologies, including the development of functional assays, had changed beyond all recognition over the past two decades. He stated:

If we synthesise a compound we can identify exactly what it is – its structure and everything else – within an hour. Previously we would send it down for carbon, nitrogen and oxygen analysis and a week later you’d be able to construct an idea of what you’ve made. Analytical technologies have all completely moved on in terms of where they were 25 years ago. That really does affect our productivity ... 25 years ago, mass spectrometry was essentially a room; a bloody big magnet that could analyse one compound every hour or so. Now a mass spec comes out quickly on a computer and you have lots of data available for analysis. These are just amazing changes (Head of Global Sciences and Information, INT2/Company B).

Here, new technologies create greater efficiency in the early-stage development of new compounds. Better information about the chemical compound and its biological target, which can be accumulated and analysed faster than ever before using a panoply of automation and data mining technologies, has enabled companies to improve decision making on which compounds to take forward for further development. However, this information explosion has also created its own R&D challenge; how best to disaggregate the data and identify the useful information that can facilitate strategic decision making.

Finally, developments in DNA Sequencing and functional analysis following the mapping of the Human Genome have led to the identification of an increasing number of potential drug targets, which include receptors, enzymes and a large number of previously unknown proteins (Dahl, 2006). Of course, new targets from cDNA sequencing (complementary DNA is DNA synthesised from a mature mRNA template) had been identified prior to the completion of the Human Genome Project. Nevertheless, the possibility of developing new therapies for thousands of drug targets, rather than the 500 or so companies had traditionally been restricted to, was extremely attractive to large firms as it broadened their options for therapeutic innovation. However, one interview respondent stated that although his own company had successfully identified a range of new biological targets, it was finding it difficult to validate the targets and develop

molecules with the right pharmacological spectrum to interact with them effectively. He stated: "What has happened is that we've had a number of efforts making molecules that don't actually do anything very exciting in the clinic" (Head of Neuroscience, INT9/Company D). Another respondent stated:

As the technology increased its stronghold in genomics, targets were being turned over very rapidly but were non-validated. This significantly impacted their efficiency and their value in a negative manner (Former Head of Computational Biology, INT8/Company C).

A major challenge for industry is to design and develop new methods and algorithms for data integration and analysis. A former head of bioinformatics at a major pharmaceutical firm stated:

Better hypothesis generation is required so you can rank your targets using the software with some plausible guesses if this type is better than others ... you need to be able to integrate information from three platforms – gene expression, proteomics and metabonomics (INT6/Company A).

Although most of the respondents did believe that new technologies had created greater efficiency in early-stage R&D, they were far more circumspect in their assessment of the downstream impact of the life sciences. One respondent claimed that although his company's discovery research groups had improved candidate selection by exploiting new technologies, "If you ask me have we got anything to show for it yet [in terms of radically new therapies], I think I'd be fibbing if I said we had" (Director of Academic Liaison, INT9/Company A). Nevertheless, this respondent was optimistic about the future potential of genomics. He claimed that the larger firms were beginning to accumulate and integrate genomic data in a way that has allowed them to begin stratifying certain diseases and their progression at the genomic level. Although it is still unclear whether the complex information derived from DNA and tissue studies will be successfully translated into useful information for therapeutic development, interview accounts revealed that all the major companies are actively collecting DNA and tissue samples and utilising biodata in conjunction with conventional wet chemistry. Pharmacogenetics is certainly still in its infancy, and may not yet have met the high expectations of downstream stakeholders and regulators (Hedgecoe and Martin, 2003), but companies appear committed to exploring its potential use in both early and late stages of drug development.

In addition to the specific development and integration of new technologies, there have also been substantial process changes in R&D. One respondent claimed that activities her company did not traditionally do in the research stage, such as toxicology, pharmacokinetics, drug deposition and pharmacodynamic modelling, are now initiated before drugs become nominated into development (VP Discovery and External Affairs, INT 4/Company B). The ultimate goal for firms is to better predict which compounds are likely to progress successfully through the various development phases of R&D. If companies can exploit new technologies and frontload some of their existing activities to improve decision making on the selection of early-stage compounds, this may help reduce the phase 2 attrition rates that continue to plague the industry.

However, there does remain a number of scientific, technological and commercial challenges to the successful exploitation and integration of new life science technologies within a conventional pharmaceutical innovation system. Interview respondents were

remarkably candid in their assessment of the various R&D bottlenecks within their companies. One respondent suggested that there had been a great deal of hype surrounding some of the technologies, which later failed to deliver on their early promise. He claimed that anti-sense technologies failed to make the grade, and RNAi use *in vivo* is still very much experimental and has an uncertain future. This respondent also argued that the Human Genome Project had been a mixed blessing in terms of developing new targets for truly innovative drugs. He stated:

We initially imagined that the human genome was going to have a lot more genes than it turned out to have. That makes a big difference because people have made estimates of the size of the druggable genome; that is, the numbers of proteins belonging to structural classes for which small molecule ligands are known (such as G protein-linked receptors or ion channels or kinases). It's not that many, probably about 10%. Three thousand targets isn't a lot when you think we've already developed drugs for 500, and of those 3000, many of them won't be involved in any way in modifying disease processes. So the pessimistic view is we've already mined it out, at least for small molecule drug discovery, or we have done all the easy ones and only the hard ones are left. If the genome had been 3 times bigger, you wouldn't have that feeling (Former Head of Neuroscience, INT9/Company D).

The comment that all the easy targets have already been exploited may partly explain why it is taking so long to develop the novel therapies that genomics promised to deliver and downstream stakeholders increasingly expect. The failure of pharmaceutical companies to market the 'designer drugs' and personalised therapies for hitherto intractable conditions (Joppi et al., 2005), which arouses much excitement amongst the media, patient groups and the public, reflects the growing complexity of the innovation pathway. The paradigm shift from traditional small-molecule-based therapies to biologics has been a slow, evolutionary process within the large firms as they struggle to collect, store and interpret the complex data available and identify commercial opportunities associated with new innovation trajectories. This partly explains why large firms have tended to pursue mergers, acquisitions and strategic alliances with smaller biotechnology firms as their primary route to biologics (see Cockburn, 2004; Mittra, 2007). Nevertheless, although there has been a trend towards increased sourcing of compounds from external innovators, as opposed to internally-driven R&D (Danzon et al., 2004; Lane and Probert, 2007), large firms continue to prioritise in-house projects where they have strong internal capabilities. Indeed, most of the large multinationals have been slowly accumulating internal knowledge, expertise and resource capabilities in biotechnology alongside traditional chemistry. The notion that large pharmaceutical firms are no longer as innovative as the smaller, entrepreneurial biotechnology companies, and perhaps incapable of developing in-house new life science based therapies, does not seem to be supported by the evidence (Schmid and Smith, 2005). One interview respondent stated:

There is this kind of urban myth that the pharmaceutical industry is only interested in small molecules and doesn't do anything else, and all the innovative stuff comes from little companies. My company is probably one of the biggest biotech companies in the sense that it makes biological drugs, and always has done, so we don't make this distinction. An appreciable part of our portfolio is proteins, peptides and humanized antibodies, with expertise developed over years through making insulin (Head of Neuroscience, INT9/Company D).

In addition to the problem of data sourcing and interoperability, and how best to identify viable commercial options for developing life science-based therapeutics, there is also a significant clinical challenge facing contemporary drug developers. As regulators and publics demand greater safety and efficacy requirements for new therapies, firms need to better integrate clinical and laboratory studies to ensure drugs have the optimal pharmacological spectrum and toxicological effects can be predicted with relative certainty. In this context, firms are exploring the potential of pharmacogenetics and trying to identify novel biomarkers, to facilitate the drug discovery process. However, this still requires the successful integration of disparate types of clinical information, knowledge and expertise; particularly chemistry, biology and information technology. Although firms appear to be developing a more diverse range of internal capabilities and interdisciplinary operating conditions, success in terms of new product output has been slow to materialise.

All the interview respondents cited the phase 2 attrition rate, and general inefficiency in the middle stages of the R&D process, as the primary challenge currently facing large firms. Two primary reasons were given for the high attrition rate and diminished productivity. Firstly, increasing expectations of safety and efficacy by regulators and healthcare providers has led to the requirement for much larger and better designed clinical trials. Problems of patient recruitment and escalating costs of clinical trials have directly affected R&D performance. Secondly, the availability of much more clinical data and genomic information, which has been welcomed by industry, has also contributed to an overall increase in the cost of drug development and slowed down certain phases of R&D. Although some parts of R&D have become more efficient, such as discovery, preclinical candidate selection and manufacturing, attrition in the middle stages of R&D has not improved a great deal. For this reason, companies have begun to fundamentally reorganise their R&D operations and management systems, as well as explore novel strategic collaborations with external innovators, to extract value from the new technologies and exploit what is now conventionally termed 'translational medicine'.

4 Experiments with new organisational models for pharmaceutical R&D and exploitation of public sector resources

In response to the opportunities and challenges engendered by life science technologies, as well as the capricious operating environment for contemporary pharmaceutical R&D, companies are exploring new organisational and strategic options for speeding up the transition of compounds from the laboratory to the clinic. In this section, I describe and critically evaluate two exemplary initiatives that illustrate some of the strategic and organisational changes taking place within the large firm sector. The first case study looks at GSK's CEDD, which represents a radical overhaul of internal R&D management. The second case study looks at Wyeth's investment in Translational Medicine through a novel Public-Private initiative located in Scotland. Although they appear to be very different cases in terms of scale and scope, and many other companies are also adopting similar strategies to a greater or lesser extent, these cases do usefully illustrate some of the managerial changes and strategic options large companies are currently experimenting with.

4.1 GSK and the CEDD

In early 2000, GlaxoSmithKline underwent a major restructuring initiative, led by its new CEO Tadataka Yamada, which culminated in a decentralised R&D model as a strategic response to the fundamental challenges of modern drug development; in particular the phase 2 attrition rate and declining productivity. This section examines the implementation of GSK's CEDD, which signalled a departure from the conventional, highly centralised and top-down R&D management model characteristic of most multinational pharmaceutical companies. The establishment of the CEDDs was an ambitious and high-risk strategy, but GSK believed that these relatively small and autonomous units, which attempt to imitate the entrepreneurial spirit of the smaller biotech companies, would facilitate the transition of compounds through its R&D pipeline. The most significant innovation was that each CEDD would be therapeutically aligned and be given decision rights and control over early-stage candidates. However, there are important questions about the overall effectiveness of the CEDD strategy, and the evolving relationships and knowledge flows between these multihub structures and remaining centralised departments within GSK (Criscuolo and Narula, forthcoming). It is important to consider the benefits and challenges of R&D diversification for innovation and strategic management.

Initially, discovery scientists at GSK were divided into six CEDDs. A seventh CEDD was created later to focus specifically on biopharmaceuticals, which signalled GSK's increasing commitment to life science innovation. More recently, GSK established a Centre of Excellence for External Drug Discovery; a virtual organisation that leverages external alliances and collaborations. The CEDD strategy emerged from Yamada's growing scepticism with the traditional big pharma model of R&D, particularly its reliance on a centralised and bureaucratic decision-making structure and the artificial boundary it constructs between the discovery and development phases of R&D. This countenances Drews and Ryser's (1996) argument that traditional pharmaceutical firms often lack the organisational and managerial flexibility required in the age of complex biomedicine. Yamada stated:

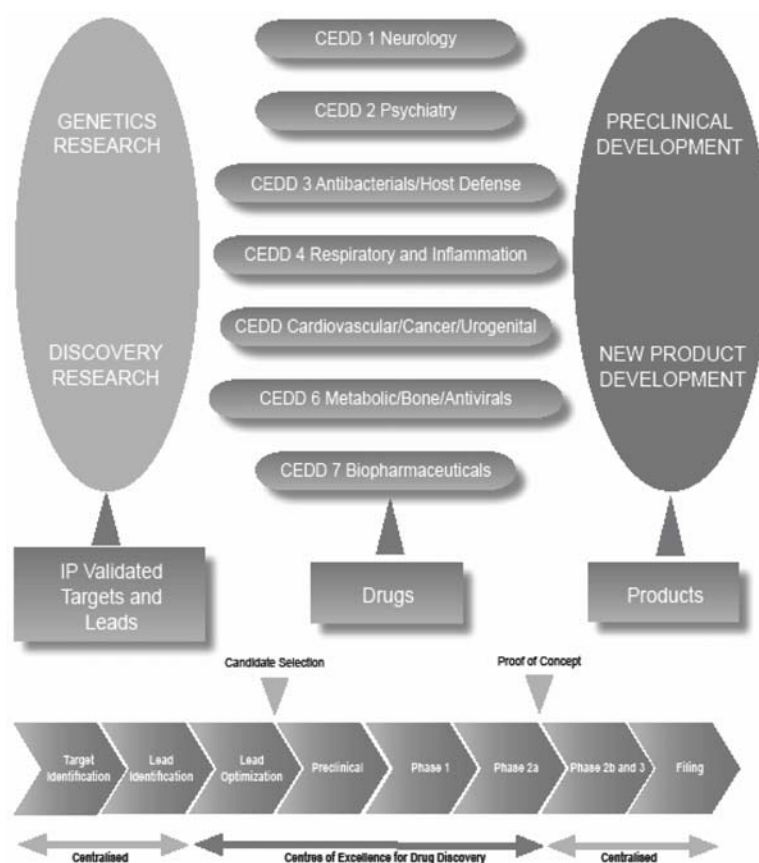
"There are times in the R&D process where you want to leverage your scale, and there are others when you want to be nimble and responsive. For example, large pharmaceutical companies are very good at the front-end of drug discovery, which often involves capital-intensive, high-throughput screening of compounds for activity against a target. They are also very good at the later stages of drug development – running large clinical trials and managing the FDA approval process. It is the important middle ground of this process – converting promising compounds into viable products – where the flexibility and responsiveness of smaller biotech firms is essential. The challenge for GSK was to put together an R&D organization that benefited from the best characteristics that big pharma and smaller biotechs had to offer." (cited in Huckman and Strick, 2005)

The basic idea was to confront the attrition and productivity problem by creating relatively independent, geographically diverse 'hub' R&D units that would acquire the functions previously held by centralised management systems for the middle stages of the R&D process.

Each CEDD is relatively small (250–350 research scientists) and headed by a senior vice president. The research scientists largely comprise biologists and chemists, but the CEDDs also include physicians and clinical researchers whose role is to contribute to the

design and implementation of preclinical and clinical trials. Clinical experts are essential for facilitating the translation of compounds into viable therapeutic products. Close collaboration between clinical experts and discovery scientists, and exploitation of bi-directional knowledge flows, allows information from preliminary human experiments to be fed back to discovery scientists (Horig and Pullman, 2004). Discovery scientists can then refine their understanding of the disease model and drug candidate and optimise the therapeutic compound for clinical use. To ensure the flexibility and responsiveness of the CEDDs, each is engineered to be small, autonomous and able to foster close day-to-day interactions amongst its scientists. If the CEDDs were too large and centrally controlled, they could become overly bureaucratic and lose the entrepreneurial spirit GSK considered essential for the middle stage of drug R&D, which involves candidate selection, preclinical/phase 1 and proof of concept studies. The basic structure of the CEDD initiative is presented in Figure 3.

Figure 3 GSK CEDD structure



Source: Created by author using company information.

In this model, scientists report directly to the leader of their CEDD, as opposed to the global functioning areas of GSK. Each CEDD identifies diseases of interest within its broad therapeutic remit and then 'commissions' GSK's centralised Genetics Research and Discovery Research departments to search for relevant targets and lead compounds.

Genetics Research identifies the molecular targets, while Discovery Research applies high-throughput screening technologies to isolate lead compounds. At the front-end of discovery, GSK also has a Technology Innovation Board (TIB), made up of senior vice presidents, which evaluates and benchmarks competing chemical and biological platform technologies for possible use by the CEDDs. The CEDDs are not obliged to accept suggested lead compounds and are permitted to license-in compounds from external innovators if it is within their available budget.

CEDDs take responsibility for projects at the stage of lead optimisation, performing chemical and biological analysis on the compound to evaluate a range of structural variations likely to meet the needs of a particular target. Once the compound has been optimised, scientists decide whether to progress the compound to preclinical animal testing. If preclinical studies are successful, the leader of the CEDD decides whether phase 1 clinical trials are to be initiated. This process is conducted independently of the centralised departments of GSK. If the compound is still considered viable once proof of concept has been established, the CEDD presents the compound to GSK's centralised Development Investment Board (DIB). This is the first point in the innovation life cycle where corporate-level R&D executives make decisions about the compound's future. If the board accepts the compound, phases 2 and 3 clinical trials are initiated. Since large pharmaceutical companies have historically been best positioned to conduct late stage clinical trials and initiate regulatory approval processes, GSK was reluctant to relinquish centralised control of this function.

It must be noted that GSK is not unique amongst the large pharmaceutical firms in organising R&D according to therapeutic areas. Furthermore, most large firms now have geographically distributed R&D facilities in what might be termed a networked 'hub structure' (Criscuolo and Narula, forthcoming). However, the managerial innovation was in the new operating norms established within the CEDDs. As one interview respondent stated:

The vast majority of large companies will split their R&D on some geographical or therapeutic area basis anyway; they don't tend to just lump it all in one building. So it's kind of a historical trend anyway. But the notion that you're giving your working people more individual responsibility and autonomy is new ... the notion was that these quasi-independent Centres of Excellence could then function to attract funding from outside the company. If they weren't getting what they wanted from discovery research or genetics research within GSK, they had a budget and they could go buy it externally (Research Scientist, INT7/Company A).

The purported autonomy to seek external alliances and collaborations, coupled with an internally competitive organisational structure, appears to distinguish the CEDDs from the more conventional decentralising strategies developed by similar sized firms.

GSK claims that reducing the layers of management between the leadership team and the bench scientists has 'enabled much earlier go/no go decisions to be made, compressing timelines and lowering costs' (GSK Annual Report, 2006). In 2003, Yamada made the following statement on GSK's website:

"Our new CEDD structure is working well. We are developing more quality compounds than ever before. This is enabling us to renew our pipeline in disease areas where we are leaders – like respiratory and psychiatry – and to build strong portfolios in areas like oncology and cardiovascular disease."

GSK clearly saw the success of the small biotechnology companies as good reason to experiment with a radically new organisational form. The attempt to create independent, competitive and close-knit research units, yet allow these networked hubs to exploit the expertise, scale and scope of a large firm's discovery and late-stage development capabilities, was a bold and ambitious strategy. However, there are a number of potential problems that may undermine this strategy's long-term success and status as a model of best practice for the industry.

Firstly, CEDDs do not contribute to discovering new targets and have a limited role in improving the safety, efficacy and market access to new therapies, functions which remain highly centralised. The challenges facing the pharmaceutical industry are much broader than mid-stage R&D and many generic problems are likely to persist, particularly the regulatory hurdles, challenges of stakeholder expectations and the low number of NCEs (relative to R&D investment) being discovered.

Secondly, the extent to which the CEDDs truly imitate the biotechnology sector is not clear. As one commentator has stated:

"To truly mimic a biotech firm, one might expect these units to be able to go off at a tangent if they find something really exciting, and look at niche drugs that might be considered too small for GSK itself to bother working on."
(Nature Biotechnology, 2001)

This does not appear to be the case at GSK, since all candidates must be approved at a higher corporate level at some point in their life cycle.

Thirdly, the competitive nature of the CEDDs, which is presented as one of the model's key strengths, could hinder GSK's ability to exploit similarities of 'mechanisms of action' across therapeutic areas, and therefore achieve economies of scope in R&D. Henderson (2000) argues that it is large, centralised firms that are generally better able to exploit internal knowledge spillovers and economies of scope in early-stage R&D. Furthermore, the benefits of spillovers can only be acquired if there is a sufficient level of 'absorptive capacity' (Cohen and Levinthal, 1990), which requires close collaboration between different sections of the research organisation. If a compound has therapeutic relevance to two disease areas located in geographically diverse and relatively autonomous CEDDs, the potential for serendipitous knowledge spillover is reduced and the model appears to lose one of the key benefits associated with a large and centralised organisational structure.

Fourthly, it is extremely difficult to evaluate the impact of the CEDDs on GSK's overall productivity. Since they were established, GSK has prosecuted an increased number of strategic alliances, small-scale acquisitions and licensing deals. These specific strategies, operated through a virtual CEDD, may have had a greater impact on productivity than the establishment of the original CEDDs. This virtual CEDD appears little different from the external knowledge management departments now common in most large firms, but its virtual nature engenders a particular problem for innovation. Since it does not conduct any basic research, and appears disconnected from the research hubs, it may not have access to sufficient knowledge and expertise to evaluate the potential of external innovations and their relevance to core CEDD activities. In most firms, research scientists are heavily involved in the development of alliances associated with their specific areas of research, but it is unclear to what extent this virtual organisation involves scientists from the main CEDDs in its decision-making processes.

Finally, the very independence of the CEDDs may have negative knock-on effects on the centralised discovery unit that feeds it with compounds. As one interview respondent stated:

If you're in discovery research and you're running a standardized process supplying leads to the CEDDs, the CEDDs are now very different in their requirements and they keep changing their requirements. So, if you're running a huge automated process, feeding something that keeps changing its mind, there is tension in the system (Research Scientist, INT7/Company A).

Although the reorganisation of GSK is still in a relatively early-stage of development, so its long-term benefits cannot be fully evaluated, it does represent a novel large-firm strategy for extracting value from new innovations and responding to the problem of innovation deficit and productivity decline. The GSK approach has been to fundamentally restructure internal operations and organisational management to expedite and improve efficiency in phase 2 development. However, another emerging strategy has been to exploit new translational processes and networked research activities through external collaboration with public sector organisations. An exemplar of this model has been the recently established TMRC, driven by the company Wyeth.

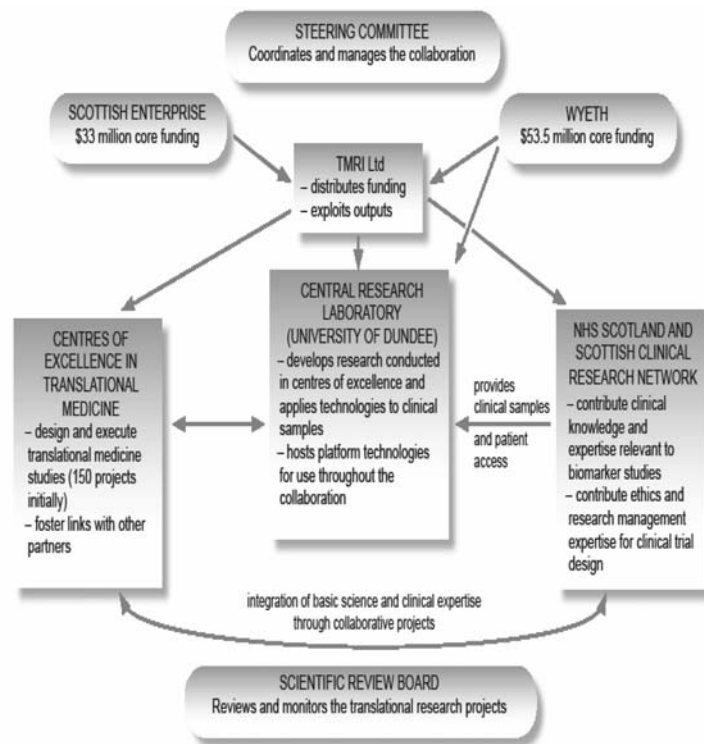
4.2 Wyeth and the TMRC

The TMRC is a broad, public–private initiative located in Scotland to extract value from translational medicine research and improve the development and delivery of innovative therapeutics. The TMRC has been described as the first of its kind, large-scale collaboration between government, academia and industry centred on Translational Medicine. The collaboration, which has initial funding of £50 million (for a five-year period between April 2006 and 2011), involves the medical schools of four of Scotland's leading research universities (Aberdeen, Dundee, Edinburgh and Glasgow); the associated cities' health boards (NHS Scotland Grampian, Greater Glasgow, Lothian and Tayside); Scotland's economic development agency, Scottish Enterprise and the global pharmaceutical company Wyeth. As successful therapeutic innovation has become increasingly difficult due to a confluence of scientific, regulatory and policy challenges; industry and the public health sector are increasingly embracing translational medicine as a potential strategy for improving the health innovation cycle.

The TMRC was established on 1 April 2006 with the broad aim to develop and exploit a world leading network of clinical and scientific excellence throughout Scotland to contribute to the discovery, development and distribution of new diagnostics and therapeutics. A major part of TMRC involves the discovery of biomarkers for the diagnosis and monitoring of human diseases. The rationale behind the public–private organisational model was recognition that successful drug development requires close interaction and sharing of knowledge and expertise between a variety of institutions involved in the complex innovation cycle – global pharmaceutical companies, research universities, healthcare providers and public funding bodies (Gambardella et al., 2000). Scotland's existing reputation for life science innovation and strong clinical infrastructure, particularly the highly integrated National Health Service and existing Networks of Clinical Excellence, helped Scotland attract the Wyeth deal (see Scottish Enterprise Report, 2005). Wyeth led the development of the collaboration in order to exploit translational medicine and biomarkers research to help it improve decision-making on its compounds.

The TMRC involves the establishment of a core research laboratory linking with four major academic Centres; as well as four NHS Trusts and Scotland's Clinical Research Network. The basic idea is to combine the resources and expertise of the various funding partners and research institutions to conduct approximately 100 translational research projects in the initial five years. Most of the individual projects are focused on basic research, but some will involve investigation-driven therapeutic interventions focused on nominated Wyeth compounds. Figure 4 illustrates the basic structure of the model and the relationships of the key organisations involved.

Figure 4 TMRC structure



Source: Created by author using publicly available information and data from interview with TMRC representative.

Wyeth and Scottish Enterprise are the two principal sponsors of TMRC. Each has provided core funding for the initial five years of the collaboration. The primary role of Scottish Enterprise is to act as facilitator and investor while Wyeth, in addition to providing core funding, will be a more active partner, using the collaboration to build on its existing expertise and commitment to translational medicine. By participating in the collaboration, Wyeth aims to,

- 1 identify groups of patients more likely to respond to a therapy
- 2 discover the optimal dosing regime for many of its products
- 3 identify and validate biomarkers to help predict drug efficacy and adverse effects.

The innovation challenge Wyeth hopes to address through its involvement in the collaboration is how best to identify the most promising drug candidates earlier in development so the cost of late-stage failure can be avoided.

The role of the four Centres of Excellence is to design and conduct the translational medicine studies. Teams of clinical and scientific researchers at each university are conducting clinical and scientific research on cardiovascular disease, neurosciences, women's health, inflammation, oncology, bone disease and diabetes. These studies are focused on the discovery and validation of relevant biomarkers. The Centres also have a leadership and governance role in developing and integrating of links between the university faculties and the collaborative partners.

The role of NHS Scotland and the Clinical Research Network is to contribute, in collaboration with the Centres of Excellence, clinical expertise and resources relevant to the biomarker studies. Furthermore, these bodies play an active role in ethics and research management, particularly in the context of clinical trials and ethical access to patient specific data and samples. Scotland's NHS has already successfully developed new standardised methods of clinical data collection, storage and analysis that can facilitate basic research, and their knowledge and expertise in clinical trial design and ethical approval is expected to make a significant contribution to the collaboration. In essence, the various NHS partners provide the important link to the patients and clinical samples that will be crucial to the success of translational medicine.

At the centre of the TMRC is the Central Research Laboratory, which is located at the University of Dundee. The laboratory's research scientists are responsible for specific laboratory-based analyses of TMRC clinical research projects carried out in the other academic centres. A major role of the laboratory is to provide a new level of standardisation to the clinical samples that are sourced via research activities at the Centres of Excellence. The laboratory also conducts tests for translational studies (these are not traditional phases 1–3 studies) sponsored specifically for the development of Wyeth compounds. The laboratory has built up strong capabilities in proteomics, analytical biochemistry and bio-informatics. The Central Research Laboratory comprises:

- 1 *a basic research laboratory*: that provides biomarker discovery, bioinformatics capabilities, assay development and core services to the other collaborating partners
- 2 *a clinical laboratory*: that conducts exploratory biomarker studies including: optimisation of biomarker assays, analytical method validation and clinical sample handling, bio-banking and processing and analyses of clinical samples
- 3 *a clinical research interface*: that connects the TMRC and the Scottish Clinical Research Network and coordinates research study design, data management and identification of external collaborators for the translational studies.

TMRI Ltd is the company that has been set up as the delivery mechanism for the collaboration. It has two main functions. Firstly, TMRI is responsible for distributing the funding from Wyeth and Scottish Enterprise to the individual organisations involved in the collaboration. Secondly, TMRI has a specific role in exploiting outputs from the collaboration. It will evaluate and market the Intellectual Property generated from the research conducted by the universities and the NHS for specific fields of use. Overall coordination and management of the collaboration and its research is conducted

by a Steering Committee and Scientific Review Board. Both have representatives from each of the collaborating partners and determine the broad strategic aims of the collaboration and approve/monitor the specific translational projects.

For Wyeth, the principal aim of TMRC is to accelerate the mid-stage drug development process so that safe and effective compounds can be more quickly and efficiently identified for late stage drug development. It hopes to achieve this through better integration of basic and clinical science. Wyeth expects to benefit from access to external resources and expertise (biomarker studies, pharmacogenetics, tissue samples and clinical trial management, etc.) to help it successfully develop in-house R&D compounds. This model provides a flexible, outsourced organisational structure to facilitate internal drug discovery and development processes. Rather than fundamentally reorganise internal organisational and management processes, as was the case at GSK, the TMRC model provides an additional strategic option run in parallel to conventional in-house R&D. Of course, the benefits of TMRC are not considered to be exclusive to Wyeth. The other partners believe that the generation of valuable IP, increased funding for scientific research, and the broader wealth creation and inward investment that will be attracted to Scotland as a result of the collaboration, will bring important public benefits.

The TMRC attempts to address a number of specific roadblocks or barriers that currently undermine successful health innovation. Two are particularly important. Firstly, for discovery research, the collaboration builds on and exploits the academic and public research base, including both basic and clinical research. The funding and support for a new, highly networked multicentred research infrastructure is expected to overcome the problem of how best to share, integrate and manage diverse public and private resources, knowledge and expertise to improve the health innovation cycle. Secondly, the problem of interoperability and integration of data is a major roadblock to successful health innovation, particularly in the context of the life sciences. The role of the Central Research Laboratory and the Centres of Excellence to develop new biomedical technologies and standardised methodologies and, in partnership with the NHS and clinical networks, to access patient data and better integrate clinical knowledge and expertise, is expected to meet this challenge. The central research laboratory is developing standardised procedures for the multicentred research projects so that, for example, the proteomics work conducted in Aberdeen uses the same methodology and validation criteria as that conducted in Glasgow.

The primary strength of the TMRC appears to be its collective and integrative strategy for developing and applying basic science and technology to promote health innovation and mitigate the phase 2 attrition rate for new compounds. By combining the resources and expertise of a major pharmaceutical company with existing publicly funded institutions, this initiative could be a potential model of best practice for translational medicine. Wyeth is not simply establishing a new R&D centre or funding a single facility or project. Rather, it is buying into a broad collaborative network that is expected to grow organically.

One potential weakness of the initiative, however, is that its organisational structure is so complex, and some of its objectives ambiguous and diverse, that it may find it difficult to deliver on its promises. The success of TMRC will depend largely on how well the participating organisations and their research staff work together on the core research projects and successfully translate the basic science into deliverable products. Furthermore, it is clear that the principal interest of Wyeth is to provide a model for

improving its mid-stage R&D efficiency, which is perhaps far less ambitious than the other public partners. While the collaboration is likely to meet the functional requirements of Wyeth, and will therefore be considered an industry success story, it is not at all certain that the broader goals of the public partners will be accomplished. There may also be a number of external factors that could undermine the success of TMRC as a potential R&D model. Drug development is, by its very nature, subject to much external uncertainty. In particular, market developments and regulatory changes might affect the success of the TMRC. These include:

- 1 more stringent, and unforeseeable, regulations on how patients may be accessed and used for clinical trials
- 2 new forms of privacy legislation to protect certain forms of clinical data, particularly genetic data
- 3 external commercial pressures on Wyeth could, potentially, affect its future commitment to TMRC.

5 Discussion and conclusions

The evolution of the pharmaceutical industry over the past two decades – driven largely by the emergence of new technological trajectories, therapeutic options and confluence of external commercial challenges – has been characterised by growing firm differentiation in terms of strategic management and organisational restructuring. There appears to be significant variation in the range and scope of individual firms' in-house capacity for biologics (Mittra, 2005), and their success in responding to the challenges of a capricious external operating environment. Although all the major pharmaceutical companies have made a significant investment in life science technologies to facilitate discovery and early stage R&D, more fundamental organisational changes and experiments with new innovation models have also been pursued by firms in response to declining productivity, inefficiencies in the middle stages of R&D, and the persistent problem of phase 2 attrition rates.

Interview accounts reveal that firms' R&D strategies and choice of therapeutic priorities are shaped by their particular histories, current research capabilities and expectations about future research trajectories. One respondent stated:

You don't start off with a blank sheet of paper. You inherit a portfolio of R&D so there is a momentum that kind of drives you to do more of the same. And companies historically have built varying portfolios. Bristol Myers Squibb always had a great strength in cancer research. Beecham essentially was an anti-infective company, so it takes a great amount of courage to move from that initial portfolio ... In terms of making investment decisions about moving into new areas or continuing in a current area, or indeed discontinuing. The most important driver is the available science and what you expect to be the available science in the average market. So companies will often make significant R&D decisions because they believe they have a particular piece of scientific capital – they've discovered a receptor or they've got a collaboration with an academic or SME that is leading them in a new way, or they've spotted something that they think no one else has ... Of course, that investment would not be allowed to proceed very far without a perceived market (Former Head of R&D Policy, INT1/Company A).

In what is a highly competitive market, firms must increasingly build on their existing capabilities and acquire a commercial advantage by developing novel therapies for a high-value market. In their evolutionary analysis of drug R&D, Tsinopoulos and McCarthy (2002) argue that individual organisations, and their particular R&D strategies, have their own particular success rate, as measured by frequency of new drugs delivered to market. Differences in success rates may provide evidence for the variation and 'fitness' of different strategies. In this context, strategies refer to R&D concentration, therapeutic focus; merger, acquisition and strategic alliance behaviour and science and technology capabilities.

However, many of the respondents admitted that companies were finding it difficult to make the paradigm shift from conventional small molecule therapies to biologics. Indeed, small molecule compounds continue to dominate large firms' R&D pipelines. Nevertheless, all agreed that the balance was slowly shifting, and that experiments with new R&D models were in some significant sense an attempt to capitalise on the emerging opportunities provided by the life sciences. Nevertheless, questions remain about the broader benefits of organisational restructuring and its implications for innovation.

The case studies of GSK and Wyeth exemplify two different strategies for responding to the current challenges of drug development and the need to better exploit the potential of the life sciences for therapeutic development. Although GSK was not unique in decentralising R&D through a networked hub structure, and reducing the size of the experimental unit, it has perhaps taken this model further than most of its major competitors. However, while such models can contribute to greater R&D efficiency and allow companies to better exploit translational processes, they can also engender 'organisational inertia' as knowledge flows and coordination follow the patterns of the antecedent structure if personnel fail to adapt to the new working practices (Criscuolo and Narula, forthcoming). Similarly, Wyeth is certainly not unique amongst the large pharmaceutical firms in developing public-private partnerships to facilitate internal R&D. Indeed, much of the research for diseases of the developing world involve partnerships between a diverse range of commercial and public research organisations and health care providers (Chataway et al., 2007). However, the novelty of the Wyeth and TMRC case study is the range of institutions involved, the basic organisational structure of the initiative and, crucially, the fact that Wyeth successfully established a long-term partnership that promises to directly contribute to resolving a range of internal R&D challenges; particularly phase 2 attrition.

However, it remains unclear whether the emergence of these new organisational models is predominantly a response to the difficulties large firms currently face, such as regulatory burdens, escalating costs of R&D and diminishing returns on investment; exhaustion of conventional science and technology; challenges to the blockbuster model of drug development, patent exposure, etc., or alternatively a revolutionary attempt to move the industry forward through a new life science-based innovation trajectory. Or perhaps the impetus for such restructuring is related, in part, to both. As the current innovation system for both conventional therapies and emerging technologies is subject to continuing turbulence, there have been shifts in the balance of power and competitive advantage within the sector (Tait and Mittra, 2004). In this context, new experimental models for science, technology and strategic management can be seen as defensive or reactionary strategies to resolve core R&D problems. However, companies do also see the positive benefits of exploiting new therapeutic options provided by genomics and

biotechnology, some of which may disrupt conventional strategies associated with small molecule R&D. In this context, decentralised R&D networks and new public–private partnerships for translational medicine can enable large firms to better utilise existing in-house capabilities, as well as build new capabilities by securing access to the knowledge, resources and expertise of external innovators.

Of course, even if the large firms can better exploit the potential of the life sciences through internal organisational restructuring or reassessment of traditional therapeutic and technological priorities and collaborative options, the social and regulatory environment for pharmaceuticals will continue to exert external pressure on firms and shape their innovation strategies. The regulatory and policy environment continues to drive strategic decision-making within firms – in this sense it occupies a powerful position outside the core innovation system (Tait, 2007) – and can have a significant effect on the type of therapies developed and their commercial value. As regulatory regimes for many technologies that could be disruptive for the pharmaceutical industry, such as stem cells, are yet to be fully developed, the strategic reorientation of some of the large multinationals are clearly not going to solve all the problems associated with innovation in the age of biomedicine. Furthermore, the new models do not necessarily have a direct impact on pricing issues, patent protection and the difficulties/costs associated with conducting large clinical trials.

Nevertheless, many of the large firms have now signalled their commitment to the life sciences and recognised key problems with the traditional, centralised R&D model. Many within industry have also expressed the belief that the traditional small-molecule blockbuster model is unsustainable. Variation within the large firm sector, in terms of how technology and therapy areas are prioritised and how R&D is managed, suggests that Big Pharma should no longer be treated as a homogenous sector. It is important to look at the specific strategies large firms are implementing, in the context of their historic capabilities and strategic vision for future R&D requirements, and evaluate them in terms of long-term impact on both early-stage efficiency and number/type of new products successfully delivered to market. Although there does appear to be a productivity crisis in the sector, the long-lead times in pharmaceutical R&D mean that the precise benefits of current restructuring initiatives will take some time to observe.

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Note

¹Primary data were derived from 11 in-depth interviews with scientists and managers who currently, or have recently, held senior management positions within large pharmaceutical companies. Four top-ten global pharmaceutical companies are represented in the sample, but due to confidentiality arrangements they are not always named in the text. Data were collected in 2005 as part of an ongoing project – conducted with the ESRC Innogen Centre, University of Edinburgh – on Innovation Processes in Life Science Industries. All respondents requested anonymity, but their area of expertise and/or job title is indicated where appropriate. Secondary data were derived from a variety of sources including: PhRMA, FDA, IMS Health, Nature Biotechnology, Deutsche Bank AG investment reports and company websites and annual reports. Data for the GSK case study were derived from company websites and publicly available data, and the TMRC case study also included an interview and extended communication with some key personnel involved in the Initiative.